



SEQUENCE LISTING

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JAN 30 2003

TECH CENTER 1600/2900

<110> Costa, M.
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Hombberger, S.

<120> ANIMAL MODELS AND METHODS FOR ANALYSIS OF LIPID METABOLISM AND SCREENING
OF PHARMACEUTICAL AND PESTICIDAL AGENTS THAT MODULATE LIPID METABOLISM

<130> 7326-101, EX99-004

<140> 09/332,522

<141> 1999-06-14

<160> 95

<170> PatentIn version 3.1

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Gln Gln Pro Asp Pro Ser Ile Pro Gly Asn Gln His Ser Pro Pro Gln
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Thr Asn Gly Pro Ser Arg Ser Lys Glu Lys Ala Ala Lys Ile Val Ile
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Gln Glu Thr Ala Glu Gly Asp Glu Asp Glu Asp Asp Glu Asp Ser Asp
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Ser Gly Glu Thr Met Ser Gln Gly Thr Thr Ile Ile Val Arg Arg Pro
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Lys Thr Glu Arg Arg Thr Ala His Asn Leu Ile Glu Lys Lys Tyr Arg
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Cys Ser Ile Asn Asp Arg Ile Gln Gln Leu Lys Val Leu Leu Cys Gly
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Asp Glu Ala Lys Leu Ser Lys Ser Ala Thr Leu Arg Arg Ala Ile Glu
385 390 395 400

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Thr Arg Thr Leu Phe Trp Glu Gly Ser Ile Ile Asn Met Ser Tyr Val
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Ile His Gly Asp Pro Val Gln Asp Phe Met Ser Val Ser Trp Gln Thr
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Phe Val Thr Thr Arg Glu Lys Ala Arg Ala Glu Leu Asn Ser Gly Asn
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Leu Lys Asp Ala Gln Arg Lys Phe Cys Glu Cys Leu Ala Thr Leu Asp
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Arg Ser Leu Pro Ser Pro Gly Val Asp Ser Val Phe Ser Val Gly Trp
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Glu Cys Val Arg His Leu Leu Asn Trp Leu Trp Ile Gly Arg Tyr Ile
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Ser His Ala Gln Thr Ala Val Leu Tyr His Glu Ile His Gln Leu His
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740 745 750

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Ala Arg Gln His Tyr Ser Leu Ile Arg Asn Cys Pro Pro Lys Ile Leu
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930 935 940

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Ser Arg Ala Ser Gly Val Val Ser Gly Ile Gln Glu Gly Thr Arg Arg

980

985

990

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His Trp His Thr Ser Ala Phe Asn Arg Thr Leu Leu Arg Trp Gly Ser
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Ala Gly Asn Ser Cys Thr Arg Arg Val Met Ile Thr Ser Phe Asn Val
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Gly Val Leu Val Thr Phe Ser Leu Leu Pro Ile Gly Leu Ile Leu Leu
85 90 95
Ile Ala Thr Ile Phe Ser Ser Gly Glu Gln Asp Ser Ser Ser Ser Val
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Glu Asp Val Pro Val Thr Gly Phe Gly Ile Lys Phe Ile Phe Cys Leu
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Pro Leu Ala Tyr Thr Glu Leu Ser His Asp His Leu Asn Ser Leu Arg
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Trp Phe Arg Lys Leu Arg Val Leu Cys Ala Gly Ile Trp His Asn Phe
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 Ser Ala Asp Phe Val Gln Leu Asn Asp Glu Ser Ser Ala Ile Ser His
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| tggcacgaat ctgaggcacc gtacaagcag actgagcaaa tcctggaggg agttccaacg | 2520 |
| caaatcgccg gacacaaaca tcgcattgaa tgcctgggtg ctgacggcgc ctacataatc | 2580 |
| agctgctgcc ttaaaggcca aatccgagtg tgggatgcac gcagtggcga gcagctaacc | 2640 |
| agcatctccc gatccgatat tcagatctct cagcagcgga cggatgggca gacgctggta | 2700 |
| cgaaagctgg ccgtgtcacc ggtctgggtgc cttgactact tcgataatct aatcgcagta | 2760 |
| ggctgcgcca acggccgcgt agaattgtgg gaatcccctg cgggattgct taagtgtgca | 2820 |

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<212> PRT
<213> *Drosophila melanogaster*

<400> 6

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Asn Ile Pro Leu Pro Gly Thr Ile Pro Thr Lys Ile Val Val Pro Tyr
 35 40 45

Glu Thr Gly Ser Gly Ser Leu Ser Trp His Ser Leu Asn Thr Ser Ser
 50 55 60

Thr Thr Pro Gln Glu Pro His Pro Ser Gly Glu Pro Trp Pro Pro Glu
 65 70 75 80

Pro Gln Val Leu Asn Ser Ser Thr Thr Asp Arg Ser Pro Pro Pro Leu
 85 90 95

Leu Pro Trp Ala Gln Ser Ser Pro Ala Phe Phe Tyr Val Gln Gln Ile
 100 105 110

Thr Leu Arg Thr Ser Val Leu Pro Trp Thr Glu Gly Met Gln Leu Met
 115 120 125

Asp Ala Phe Arg Ala Pro Leu His Glu Val Phe Lys Leu Leu Glu Ile
 130 135 140

Val Arg Asn His Gln Ser Ser Glu Asn Lys Arg Thr Leu Glu His Asn
 145 150 155 160

Cys Leu His Val Asp Asn Val Lys Arg Gly Thr His Gly Gln Leu Asp
 165 170 175

Gln Ile Phe Pro Glu Tyr Gly Cys Leu Leu Leu Ser Pro Ala Asn Leu
 180 185 190

Trp Thr Gln Asn Ser Gln Asn Phe Thr Arg Asp Thr Asn Ile Leu Asn
 195 200 205

Thr Ile Phe Gln Tyr His Asn Leu Gln Lys Ser Lys Val Ser Ala Ala
 210 215 220

Glu Met Leu Phe Gly Leu Pro Met Gln Asp Thr Gly Phe Lys Arg Tyr
 225 230 235 240

Pro Leu Arg Ala Arg Ser Arg Ile Ile Gln Tyr Ala Leu Thr Leu Phe

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 245 | | | | | | | | 250 | | | | 255 | | | |
| Leu | Lys | His | Asn | Asp | Met | Glu | Tyr | Leu | Asp | Thr | Leu | Lys | Glu | Lys | Leu |
| | | | 260 | | | | 265 | | | | | | 270 | | |
| Leu | Arg | His | Tyr | Pro | Pro | Leu | Pro | Leu | Ala | Ser | Ala | Ser | Ala | Glu | Glu |
| | | | 275 | | | | 280 | | | | | | 285 | | |
| Pro | Thr | Thr | Ile | Thr | Tyr | Ile | Phe | Tyr | Pro | Gly | Glu | Tyr | Arg | Met | Trp |
| | | | 290 | | | | 295 | | | | | | 300 | | |
| Glu | Leu | Val | Pro | Tyr | Thr | Val | Ala | Phe | Met | Leu | Val | Phe | Ala | Tyr | Val |
| 305 | | | | 310 | | | | | | 315 | | | 320 | | |
| Tyr | Phe | Ser | Val | Arg | Lys | Ile | Asp | Val | Phe | Arg | Ser | Arg | Phe | Leu | Leu |
| | | | 325 | | | | | | 330 | | | 335 | | | |
| Ala | Leu | Cys | Ser | Val | Ile | Thr | Thr | Ala | Gly | Ser | Leu | Ala | Met | Ser | Leu |
| | | | 340 | | | | | | 345 | | | 350 | | | |
| Gly | Leu | Cys | Phe | Phe | Phe | Gly | Leu | Thr | Ile | Ser | Leu | Gln | Ser | Lys | Asp |
| | | | 355 | | | 360 | | | | | | 365 | | | |
| Ile | Phe | Pro | Tyr | Leu | Val | Ile | Leu | Val | Gly | Leu | Glu | Asn | Ser | Leu | Val |
| | | | 370 | | | 375 | | | | | | 380 | | | |
| Ile | Thr | Lys | Ser | Val | Val | Ser | Met | Asp | Glu | Thr | Phe | Asp | Val | Lys | Ile |
| 385 | | | | 390 | | | | | | 395 | | | 400 | | |
| Arg | Val | Ala | Gln | Ala | Leu | Ser | Lys | Glu | Gly | Trp | His | Ile | Ser | Lys | Thr |
| | | | 405 | | | | | | 410 | | | 415 | | | |
| Leu | Leu | Thr | Glu | Ile | Thr | Ile | Leu | Thr | Ile | Gly | Leu | Ala | Thr | Phe | Val |
| | | | 420 | | | | | | 425 | | | 430 | | | |
| Pro | Val | Ile | Gln | Glu | Phe | Cys | Ile | Phe | Ala | Ile | Val | Gly | Leu | Leu | Ser |
| | | | 435 | | | | | | 440 | | | 445 | | | |
| Asp | Phe | Met | Leu | Gln | Met | Leu | Leu | Phe | Ser | Thr | Ile | Leu | Ala | Met | Asn |
| | | | 450 | | | 455 | | | | | | 460 | | | |
| Ile | Lys | Arg | Thr | Glu | Tyr | Thr | Ala | Glu | Ala | Lys | His | Leu | Pro | Lys | Met |
| 465 | | | | 470 | | | | | | 475 | | | 480 | | |

Leu Leu Ser Cys Thr Gln Gly Ala Gly Arg Gln Asp Phe Arg Phe Phe
485 490 495

Gly Ala Ala Pro Ala Leu Pro Pro Phe Val Pro Gly Thr Phe Gln Arg
500 505 510

Ser Gln Ser His Pro Lys Leu Cys Phe Ala Asp Pro Ala Ser Val Ser
515 520 525

Asp Arg Thr Ser Leu Val Asn Gly His Ser Ser Pro Glu Gln Arg Ile
530 535 540

Pro Lys Arg Ile Lys Ile Val Asn Phe Trp Ala Arg Thr Arg Phe Phe
545 550 555 560

Gln Arg Ala Phe Met Ile Trp Met Ile Val Trp Ile Cys Ser Ile Val
565 570 575

Tyr Asn Ser Gly Tyr Leu Glu Gln Leu Phe Ser Met Gln Ser Asn Gly
580 585 590

Thr Met Thr Ala Thr Leu Glu Leu Gln Arg Arg Leu Gln Ala Gly Arg
595 600 605

Gly Ala Val Ser Ser Phe Phe Glu Gly Trp Gln Ala Asp Gly Gln Arg
610 615 620

Ala Thr Ser Ala Pro Ser Gly Ser Gly Phe Ser Thr Pro Ile Lys Ala
625 630 635 640

Pro Leu Ala Ile Asp Ile Asn Glu Thr Ala Glu Glu Met Met Arg Leu
645 650 655

Arg Tyr Pro Ser Phe Asp Leu Asn Tyr Phe Leu Ser Asn Phe His Trp
660 665 670

Ser Thr Ile Met Lys Gln Tyr Asn Ile Ser Leu Ser Gly His Tyr Val
675 680 685

Thr Leu Leu Pro Thr Ile Arg Leu Ser His Ala Ile Ala Pro Glu Leu
690 695 700

Ala Thr Leu Leu Arg Asn Pro Gln Glu Gln Leu Gln Gln Asn Phe Gln
705 710 715 720

Trp Lys Ala Leu Ala Ala Ala Leu Asp Pro Leu Asp Phe Asn Asp Asp
725 730 735

Asp Val Arg Arg Glu Ser Pro Met Val Met Ala Glu Gly Leu Pro Leu
740 745 750

Val Pro Lys Ser Pro Met Glu Ile Phe Phe Ala Ile Leu Leu Cys Cys
755 760 765

Ile Ser Ile Phe Val Leu Cys Tyr Thr Met Val Val Phe Tyr Arg Cys
770 775 780

Ile Cys Thr Arg Asn Tyr Ala Glu Trp Arg Ser Ser Trp His Glu Ser
785 790 795 800

Glu Ala Pro Tyr Lys Gln Thr Glu Gln Ile Leu Glu Gly Val Pro Thr
805 810 815

Gln Ile Ala Gly His Lys His Arg Ile Glu Cys Leu Val Ser Asp Gly
820 825 830

Ala Tyr Ile Ile Ser Cys Cys Leu Lys Gly Gln Ile Arg Val Trp Asp
835 840 845

Ala Arg Ser Gly Glu Gln Leu Thr Ser Ile Ser Arg Ser Asp Ile Gln
850 855 860

Ile Ser Gln Gln Arg Thr Asp Gly Gln Thr Leu Val Arg Lys Leu Ala
865 870 875 880

Val Ser Pro Val Trp Cys Leu Asp Tyr Phe Asp Asn Leu Ile Ala Val
885 890 895

Gly Cys Ala Asn Gly Arg Val Glu Leu Trp Glu Ser Pro Ala Gly Leu
900 905 910

Leu Lys Cys Ala Tyr Gln Glu Asp Ala Lys Arg Asn Gln Gly Ile Thr
915 920 925

His Ile His Leu Asn Gly Asp Arg Val Ile Val Ala Arg Leu Asn Gly
 930 935 940

Arg Leu Asp Phe Tyr Arg Leu Glu Thr Tyr Tyr Lys Gly Lys Gln Ile
 945 950 955 960

Asp Trp Gly Phe Thr Ser Ala Tyr Arg Arg Thr His Val Arg Thr Gly
 965 970 975

Ser Thr Gly Ser Leu Gly Leu Met Leu Gln Gln Gln Arg Cys Gln Gln
 980 985 990

Glu Ala Ser Gln Lys Thr Thr Lys Glu Glu Met Lys Ile Thr Leu Glu
 995 1000 1005

Gly Val Arg Leu Ala His Gln Gln Pro Ile Thr Cys Met Gln Val
 1010 1015 1020

Val Asn Asp Met Val Phe Thr Gly Ser Gln Asp His Thr Leu Lys
 1025 1030 1035

Val Tyr Cys Leu Asn Lys Ser Asp Val Glu Tyr Thr Leu His Gly
 1040 1045 1050

His Cys Gly Pro Val Thr Cys Leu Phe Val Asp Arg Trp Gln Pro
 1055 1060 1065

Gly Thr Gly Gly Ser Gly Ser Gln Asp Gly Leu Leu Cys Val Trp
 1070 1075 1080

Asp Leu Phe Thr Gly Ala Cys Met Tyr Asn Ile Gln Ala His Asp
 1085 1090 1095

Gly Ala Val Ser Cys Leu Ala Cys Ala Pro Ser Tyr Val Ile Ser
 1100 1105 1110

Leu Gly Thr Asp Glu Arg Ile Cys Val Trp Glu Arg Phe Gln Gly
 1115 1120 1125

Asn Leu Leu Thr Thr Ile Asn Ile Ser Asn Ala Tyr Ser Ser Leu
 1130 1135 1140

Leu Met Leu Thr Pro Ser Leu Leu Val Thr Ser Lys Met Gly Lys

| | | | | |
|---|--|------|--|------|
| 1145 | | 1150 | | 1155 |
| Ala Ser Phe Leu Ile Ala Asn Ile Arg Gly Thr Val Asn Asn Lys | | | | |
| 1160 | | 1165 | | 1170 |
| Phe Asn Ser Asn Thr Gly Ser Leu Ile Val Trp Asp Val Arg Thr | | | | |
| 1175 | | 1180 | | 1185 |
| Gly Gln Pro Ala Arg Glu Val Lys Leu Asp Phe Ala Asn Leu Gln | | | | |
| 1190 | | 1195 | | 1200 |
| Leu Cys Pro Lys Ile Met Met Leu Ala Cys Asp Ser Val Val Cys | | | | |
| 1205 | | 1210 | | 1215 |
| Asp Tyr Gly Asn Glu Ile Arg Val Val Arg Phe Pro Ile Val Ala | | | | |
| 1220 | | 1225 | | 1230 |
| Asp Lys Cys His | | | | |
| 1235 | | | | |

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 <212> DNA
 <213> *Drosophila melanogaster*

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 ggaaaaacaa aagcacacgt gaactaagaa aacagataga aggtggtaaa gcattcgcaa 180
 tggacacgac actgatgaac ttaatagacg ctccgctgga cgagtccatg gatttgttca 240
 aagcggagga tgtcttcgaa ccgttcgacg ccgacctgca ctcgacatg ctggacatca 300
 tcctcaacga catggacctg gcgccgacgc agatgtacaa catgctgctg gacgagcctc 360
 gaacgcatac ccagcagacg cagtccgtgg atcagcagcc gcaatccgtc gagcaacagc 420
 cgcacgtgaa aagcgagcac tcttcgccag tgcacatcaa ggaggaactg catcagcagc 480
 aacaacagtc gccgcttctc gtctacaaac cagatcccct catagccaca agctacaatt 540
 gtccccagca acagccgacg ggccttttga aggccgccca accaacagcc accatacatc 600
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 gctttgtcta ccagtccatg tccccgccca cgtcgccggt ggagtctgcg aaccagaatg 720

| | | | | | | |
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| tcaatgtcat | gcagcccggt | gctgcaactc | ctgctccgc | ttctgctcct | ttgccccagc | 780 |
| agtcgtatcc | gcaacccttc | attacgtaca | actctaaggc | cggaatgact | tccgatgaag | 840 |
| ccatgtactt | gctcttgag | cccacggtag | ccagtcacaac | cccatctcca | cctgtggctc | 900 |
| caccaccgac | aagcacaggt | agtcggggcca | gcaaggtgcg | agtggcacca | ctggctccgt | 960 |
| cacctgccgc | tatggaagtc | cagggcaagg | tacctatcaa | ccgggttcaa | cccaaggtga | 1020 |
| aggaagtaaa | gcgctcggcc | cacaacgcca | tcgagcggcg | ctatcgacc | tcaatcaacg | 1080 |
| acaagattaa | cgagttgaag | aacttggtag | tgggagagca | ggccaagctg | aacaagtccg | 1140 |
| cagtgttgcg | gaaatccata | gacaagattc | gggatctgca | acgccagaat | cacgatctga | 1200 |
| aggcagagtt | gcagcgctg | cagagggagc | taatggcacg | cgacggctcc | aaggtgaagg | 1260 |
| atttacttca | gctgggcact | cggcctggta | gagcatccaa | gaagcgccgc | gagagctcgc | 1320 |
| agacctttac | cacggatgcc | ggactgacgc | cgccacgcag | cgatgaatcg | gaccttccgc | 1380 |
| tctcgcccat | gcactcggac | atctcgttgc | cgccatcacc | ctatggtgga | tccaccgcca | 1440 |
| gctgtagcag | tggcagcagc | agcagcaatg | aagaaccact | ggtggtgccc | agctctatgc | 1500 |
| gcggcatggc | cacccactct | cgctcggac | tctgcatgtt | tatgttcgcc | atcctggccg | 1560 |
| tcaatccctt | caagaccttt | ctccagcgcg | gccactatga | cagtaatgac | gatcttggcg | 1620 |
| acatgagcgg | tcaaagacgc | attctctctt | acgacgtgga | aggtgaaggt | tttgctgtct | 1680 |
| ggcagcagag | ttcctggata | tggctattga | acttcacact | gatgcttggga | tgcttgggtga | 1740 |
| aattgctggt | ttacggtgat | ccgcagctgg | acgcgcaaac | ggacgcctac | tgccagcaca | 1800 |
| ggcagcgggc | tgactttctat | tttagccaag | gacagtcgtc | tcaggcctac | gccggttacc | 1860 |
| tcaactgtct | gcatatgttt | ggattaagtc | taccggcgtc | gcgcttggag | tgttacttgc | 1920 |
| agaccacgtg | gcagttcctt | cgttttcttt | tccatcgctt | ctggctgggt | cgggtgctgt | 1980 |
| cacggcggtc | cgggtgggctg | tttagcaacg | ccgccagcag | gaaacaggcg | ctggcatctg | 2040 |
| cacgcgaact | ggccttgcgc | ttcaaccgac | tgaatcaatt | gcaactgact | ggaaatggaa | 2100 |
| gccgcggtga | catgaacggc | attatgatgg | cactattcgc | aagcaacatg | gctgaagtgg | 2160 |
| cgcacaatct | actgacaccg | cgcgagacca | tctgcatcca | cgtaatgaca | gcgttgcgaa | 2220 |
| tgaagcgcag | tgccccaaaa | tggttgcaac | agttcttcgc | ccgatactac | atgagccggg | 2280 |
| ctcgtcaaga | gtgcggtcgc | actagggcca | ccgagcaaac | gcaggagcta | cgttgggcat | 2340 |
| tcacagccta | tggatatcgc | tactgcgcca | cgcacgtctt | cacgtacgat | ctgagcgact | 2400 |
| ccggcgagca | ggatggattc | ttcacacgtc | ttaggaatcc | atgtgatccc | gctgcccacg | 2460 |

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<210> 8
 <211> 1113
 <212> PRT
 <213> *Drosophila melanogaster*

<400> 8

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| 1 | | | | 5 | | | | 10 | | | | | | 15 | |

Met Asp Leu Phe Lys Ala Glu Asp Val Phe Glu Pro Phe Asp Ala Asp
20 25 30
Leu His Ser Asp Met Leu Asp Ile Ile Leu Asn Asp Met Asp Leu Ala
35 40 45
Pro Thr Gln Met Tyr Asn Met Leu Leu Asp Glu Pro Arg Thr His Thr
50 55 60
Gln Gln Thr Gln Ser Val Asp Gln Gln Pro Gln Ser Val Glu Gln Gln
65 70 75 80
Pro His Val Lys Ser Glu His Ser Ser Pro Val His Ile Lys Glu Glu
85 90 95
Leu His Gln Gln Gln Gln Gln Ser Pro Leu Leu Val Tyr Lys Pro Asp
100 105 110
Pro Leu Ile Ala Thr Ser Tyr Asn Cys Pro Gln Gln Gln Pro Thr Gly
115 120 125
Leu Leu Lys Ala Ala Gln Pro Thr Ala Thr Ile His His Met Asp Ala
130 135 140
Gln Arg Met Pro Pro Asn Thr Ala Val Tyr Pro Pro Ser Leu Gly Ser
145 150 155 160
Ser Phe Val Tyr Gln Ser Met Ser Pro Pro Thr Ser Pro Val Glu Ser
165 170 175
Ala Asn Gln Asn Val Asn Val Met Gln Pro Val Ala Ala Thr Pro Ala
180 185 190
Pro Ala Ser Ala Pro Leu Pro Gln Gln Ser Tyr Pro Gln Pro Phe Ile
195 200 205
Thr Tyr Asn Ser Lys Ala Gly Met Thr Ser Asp Glu Ala Met Tyr Leu
210 215 220
Leu Leu Gln Pro Thr Val Ala Ser Pro Thr Pro Ser Pro Pro Val Ala
225 230 235 240
Pro Pro Pro Thr Ser Thr Gly Ser Arg Ala Ser Lys Val Arg Val Ala

245 250 255
 Pro Leu Ala Pro Ser Pro Ala Ala Met Glu Val Gln Gly Lys Val Pro
 260 265 270
 Ile Asn Arg Val Gln Pro Lys Val Lys Glu Val Lys Arg Ser Ala His
 275 280 285
 Asn Ala Ile Glu Arg Arg Tyr Arg Thr Ser Ile Asn Asp Lys Ile Asn
 290 295 300
 Glu Leu Lys Asn Leu Val Val Gly Glu Gln Ala Lys Leu Asn Lys Ser
 305 310 315 320
 Ala Val Leu Arg Lys Ser Ile Asp Lys Ile Arg Asp Leu Gln Arg Gln
 325 330 335
 Asn His Asp Leu Lys Ala Glu Leu Gln Arg Leu Gln Arg Glu Leu Met
 340 345 350
 Ala Arg Asp Gly Ser Lys Val Lys Asp Leu Leu Gln Leu Gly Thr Arg
 355 360 365
 Pro Gly Arg Ala Ser Lys Lys Arg Arg Glu Ser Ser Gln Thr Phe Thr
 370 375 380
 Thr Asp Ala Gly Leu Thr Pro Pro Arg Ser Asp Glu Ser Asp Pro Ser
 385 390 395 400
 Leu Ser Pro Met His Ser Asp Ile Ser Leu Pro Pro Ser Pro Tyr Gly
 405 410 415
 Gly Ser Thr Ala Ser Cys Ser Ser Gly Ser Ser Ser Ser Asn Glu Glu
 420 425 430
 Pro Leu Val Val Pro Ser Ser Met Arg Gly Met Ala Thr His Ser Arg
 435 440 445
 Leu Gly Leu Cys Met Phe Met Phe Ala Ile Leu Ala Val Asn Pro Phe
 450 455 460
 Lys Thr Phe Leu Gln Arg Gly His Tyr Asp Ser Asn Asp Asp Leu Gly
 465 470 475 480

Asp Met Ser Gly Gln Arg Arg Ile Leu Ser Tyr Asp Val Glu Gly Glu
 485 490 495

Gly Phe Ala Val Trp Gln Gln Ser Ser Trp Ile Trp Leu Leu Asn Phe
 500 505 510

Thr Leu Met Leu Gly Cys Leu Val Lys Leu Leu Val Tyr Gly Asp Pro
 515 520 525

Gln Leu Asp Ala Gln Thr Asp Ala Tyr Cys Gln His Arg Gln Arg Ala
 530 535 540

Asp Phe Tyr Phe Ser Gln Gly Gln Ser Ser Gln Ala Tyr Ala Gly Tyr
 545 550 555 560

Leu Asn Cys Leu His Met Phe Gly Leu Ser Leu Pro Ala Ser Arg Leu
 565 570 575

Glu Cys Tyr Leu Gln Thr Thr Trp Gln Phe Leu Arg Phe Leu Phe His
 580 585 590

Arg Leu Trp Leu Gly Arg Val Leu Ser Arg Arg Ser Gly Gly Leu Phe
 595 600 605

Ser Asn Ala Ala Ser Arg Lys Gln Ala Leu Ala Ser Ala Arg Glu Leu
 610 615 620

Ala Leu Leu Phe Asn Arg Leu Asn Gln Leu Gln Leu Thr Gly Asn Gly
 625 630 635 640

Ser Arg Gly Asp Met Asn Gly Ile Met Met Ala Leu Phe Ala Ser Asn
 645 650 655

Met Ala Glu Val Ala His Asn Leu Leu Thr Pro Arg Glu Thr Ile Cys
 660 665 670

Ile His Val Met Thr Ala Leu Arg Met Lys Arg Ser Ala Pro Lys Trp
 675 680 685

Leu Gln Gln Phe Phe Ala Arg Tyr Tyr Met Ser Arg Ala Arg Gln Glu
 690 695 700

Cys Gly Arg Thr Arg Ala Thr Glu Gln Thr Gln Glu Leu Arg Trp Ala
 705 710 715 720

Phe Thr Ala Tyr Gly Tyr Arg Tyr Cys Ala Thr His Val Phe Thr Tyr
 725 730 735

Asp Leu Ser Asp Ser Gly Glu Gln Asp Gly Phe Phe Thr Arg Leu Arg
 740 745 750

Asn Pro Cys Asp Pro Ala Ala His Val Ile Lys Gln Tyr Arg Glu His
 755 760 765

Leu Leu Phe Lys Ser Ile Gln Cys Leu Val Gly Ala Gly His Lys Ser
 770 775 780

Gly Gly Leu Pro Thr Ser Ser Val Ser Gly Glu Ala Glu Gln Leu Gln
 785 790 795 800

Gln Gln Gln His Ser Gly Thr Ile Val Ser Asn Val Leu Lys Tyr Thr
 805 810 815

Ser Leu Leu Lys Asp Thr Leu Trp Ala Asp Glu Asp Glu Arg Asp Thr
 820 825 830

Asn Val Val Trp Trp Ala Asp Val Leu Glu Thr Ala Val His Trp Leu
 835 840 845

Leu Gly Glu Asp Thr Leu Ala Glu Gln Leu Tyr Gly Arg Ile Lys Gln
 850 855 860

Met Pro Thr Gln Leu Gln Gln Cys Gly Glu Asn Asp His Leu Pro Lys
 865 870 875 880

Ala Leu His Ala Val Leu Arg Ala Lys Met Ile Leu Leu Lys Asn Asn
 885 890 895

Gly Asn Ala Leu Asp Lys Ser Leu Lys Gln Leu Val Asn Ile Leu Cys
 900 905 910

Asp Glu Ser Ser Val Glu Leu Gln Glu Cys Leu Thr Val Asn Arg Ile
 915 920 925

Thr Asp Ala Lys Gly Ile Lys Leu Leu Phe Gln Leu Leu Thr Cys Asp
 930 935 940

Trp Leu Leu Glu Thr Arg Thr Ala Leu Trp Glu Leu Glu His Met Asn
 945 950 955 960

Met Glu Asp Asp Gly Phe Tyr Gln Val Pro Gly Glu Val Leu Glu Lys
 965 970 975

Phe Gln Thr Asp Leu Asn Ser Leu Arg Asn Ile Val Glu Asn Ile Pro
 980 985 990

Asn Ala Gln Ser Arg Ile Tyr Leu Tyr Glu Ala Val Cys Arg Leu Met
 995 1000 1005

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Leu Arg Ser Arg Asn Ala His Ser Ser Ile Phe Cys Gly Ser Lys
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Asp Arg Arg Gln Gln Asn Phe Val Gly Gly Glu Arg Glu Arg Ala
 1040 1045 1050

Ser Ala Met Tyr Val Ala Cys Lys Tyr Leu Pro Pro Ala Leu Leu
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Ser Ser Pro Gly Glu Arg Ala Gly Met Leu Ala Glu Ala Ala Lys
 1070 1075 1080

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Thr Phe Val Gln Val Tyr Phe His Pro Leu Lys Thr Phe Ser Asp Tyr
260 265 270

Ile Pro Leu Ile Ser Thr Tyr Phe Val Cys Met Ile Tyr Val Tyr Tyr
275 280 285

Ser Ser Arg Lys Ile Gln Met Val Ala Ser Arg Trp Gly Leu Ala Phe
290 295 300

Ala Ser Ser Phe Thr Val Ala Ser Thr Leu Leu Met Thr Thr Gly Ile
305 310 315 320

Cys Ala His Leu Asp Leu Ser Thr Thr Thr Trp Gly Ser Glu Val Tyr
325 330 335

Pro Tyr Ile Ala Leu Ile Met Gly Leu Glu Asn Thr Leu Cys Ile Thr
340 345 350

Arg Ser Val Val Tyr Thr Ser Pro Ser Leu Asp Val Ser Ser Arg Ile
355 360 365

Ala His Gly Leu Ser Gln Glu Gly Tyr Lys Leu Thr Lys Tyr Tyr Ile
370 375 380

Leu Glu Leu Leu Ala Leu Leu Ile Gly Phe Leu Thr Arg Ile Ser Asp
385 390 395 400

Ile Gln Glu Phe Cys Gln Phe Ser Val Ile Cys Val Thr Val Asp Phe
405 410 415

Tyr Met Gln Leu Phe Phe Tyr Ala Pro Cys Leu Thr Phe Asp Leu Gln
420 425 430

Arg Leu Gly Leu Glu Glu Lys Arg Lys Phe Ala Glu Ile Leu Leu Tyr
435 440 445

Glu Glu Ile Pro Arg Leu Lys Asn Tyr Ala Pro Val Ser Cys Pro Met
450 455 460

Arg Lys Ile Trp Pro Lys Leu Phe Val Met Lys Lys Met Gln Lys Arg
465 470 475 480

Arg Val Ser Asp Ser Gly Ile Glu Asp Val Met Lys Asn Asp Glu Gln
485 490 495

Arg Arg Leu Leu Ile Ser Ser Glu Phe Asp Ser Lys Asp Asp Gly Asp
500 505 510

Val Gln Glu Pro Arg Pro Glu Asp Ser Val Arg Met Lys Ile Met Tyr
515 520 525

Phe Ile Thr Arg Thr Arg Ile Val Gln Arg Thr Ile Leu Val Val Phe
530 535 540

Ala Ile Trp Thr Val Phe Leu Val Phe Phe Val Gly Ser Arg Gln Leu
545 550 555 560

Gly Met Glu Ser Asn Leu Thr Ser Lys Leu Trp Pro Pro Val Ala His
565 570 575

Glu Tyr Asn Ile Ser Leu Asn Ser Arg Tyr Val Thr Phe Leu Pro Pro
580 585 590

Ile Val Ile Asn Ala Ile Val His Pro Thr Asp Ile Leu Leu Gln Asn
595 600 605

Val Glu Lys Thr His Val Asn Val Pro Asn Glu Glu Glu Asp Ala Pro
610 615 620

Ile Leu Arg Ser Arg Ile Asp Trp Leu Glu Met Gln Leu Lys Met Tyr
625 630 635 640

Leu Ala Ala Phe Trp Leu Leu Leu Ile Thr Thr Val Ile Ser Phe Phe
645 650 655

Ala Tyr Val Phe Leu Ile Asp Arg Trp Lys Leu Arg Gly Val Lys Gln
660 665 670

Ile Gln Glu Gln Gln Met Ser Glu Thr Thr Thr Asp Ser Ser Glu Thr
675 680 685

Val Lys Asn Phe Val Asp Thr Leu Pro Ile Val Tyr Gln Gly His Arg
690 695 700

Phe Pro Ile Glu Ser Val Ala Ile Asp Pro Glu Asp Thr Ser Thr Phe
705 710 715 720

Val Ser Cys Cys Gln Glu Gly Val Val Tyr Val Trp Asn Thr Gln Thr
725 730 735

Gly Gln Arg Thr Leu Arg Ile Asn Arg Leu Arg Ala Val Pro Glu Lys
740 745 750

Gly Lys Glu Ile Pro Ser Ala Pro Lys Ile Trp Ala Ile Ala Lys Arg
755 760 765

His Phe Phe Ser Asn Thr Thr Ser His Val Val Cys Arg Glu Asp Asp
770 775 780

Val Ala Val Val Arg Leu Asp Gly Ser Ile Glu Phe Leu Arg Ile Asp
785 790 795 800

Tyr Asp Arg Thr Asp Gly Thr Ile Arg Val Arg Lys Ile Glu Leu Leu
805 810 815

Lys Ser Val Arg Ala His Gln Lys Pro Val Cys Arg Ile Ala Ile Trp
820 825 830

Lys Ser Gln Leu Ile Thr Ser Ser Phe Asp Arg Ser Ile Lys Met Trp
835 840 845

Asn Trp Ala Glu Asn Pro Glu Gln Ile Asp Ile Ser Asn Val Phe Leu
850 855 860

Ala His Asn Ser Pro Val Val Asn Leu Ala Val Asp Glu Ala Thr Ser
865 870 875 880

Ile Met Tyr Ser Ser Cys Glu Glu Gly Val Ile Cys Trp Trp Asn Leu
885 890 895

Asn Thr Gly Glu Leu Ile Arg Thr Asn Asp Asn Asn Tyr Thr Trp Ala
900 905 910

Phe Gln Leu Ala Thr Ser Ser Asp Tyr Leu Leu Gly Phe Tyr Gly Ser
915 920 925

Ser Gln Leu Tyr Met Trp Asn Val Glu Asn Gly Gln Leu Ala Cys Arg

930 935 940
 Val Ser Asp Ala Leu Gly Asp Gly Thr Ser Glu Asp Thr Leu Tyr Thr
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 Ile Gly Lys Val Lys Leu Asn Gly Lys Ile Ser Ser Met Arg Lys Asn
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 35 40 45

 Arg Arg Leu Gln Ile Phe Gly Ala Gly Ile Trp His Asn Leu Leu Leu
 50 55 60

 Ala Leu Leu Ala Met Xaa Met Phe His Ala Ser Pro Val Ile Leu Ser

65

70

75

80

Pro Val Leu Ala Asn Gly Tyr Xaa Val Ser Val Arg Gly Val Asp Val
85 90 95

Arg Ser Xaa Leu Ser Asn Pro Arg Thr Gly Leu Val Ala Gly Asp Val
100 105 110

Val Lys Ser Val Asp Glu Cys
115

4